

**REMARKS**

Reconsideration and withdrawal of all rejections is respectfully requested in view of the above-provided amendments and the following remarks.

Claims 55, 57-58, 61-75, 77-109 are pending. Claims 72-73 and 99-109 have been withdrawn from active prosecution by the Examiner as directed to non-elected subject matter. Claims 56, 59-60 and 76 are newly cancelled, without prejudice.

**AMENDMENTS TO THE CLAIMS**

Claim 55 is amended to incorporate the limitations of claims 56 and 60. At part (c), claim 1 is amended to copy the term, "solution" from the last clause of the same claim, to provide a proper antecedent basis for the last clause of claim 1. The artisan would appreciate that a buffer with a measurable pH is in solution, and this also conforms to claim 88. Claims depending from claim 55 are cancelled or conformed, as appropriate. Claims 68 and 69 are amended to depend from claim 55, instead of from claim 67, to address the Examiner's objection to the scope of these claims.

Claims 74 and 97 are amended to remove the Markush group, leaving the subgenus covering the specific elected species, as required by the Examiner.

Claim 86, et seq. are amended to more clearly conform to claim 55, as amended.

Claims 62, 63, and 98 are amended to remove informalities.

No new matter is added.

**THE CLAIM OBJECTIONS**

Claims 74, 76 and 97 were objected to by the Examiner for reciting non-elected subject matter, in view of "the election of the formula on page 14 of the 11/23/2009 response..." Claims 74, 76 and 97 are amended to remove the other branched polymers and to leave the subgenus compound shown on page 14 of the 11/23/2009 response.

The Examiner has also objected to claim 59 under 37 CFR 1.75(c) as allegedly in improper dependent form for failing to further limit an antecedent claim. Claim 59 is cancelled, thus obviating this ground of objection.

The Examiner objected to claims 68-69 under 37 CFR 1.75(c) as allegedly in improper dependent form for failing to further limit an antecedent claim. The Examiner pointed to the

differing scope of the Markush language between claim 67 and claims 68-69. Claims 68-69 are now amended to depend directly from claim 55, thus obviating this ground of objection.

For all of these reasons, reconsideration and withdrawal of these grounds of objection is respectfully requested.

### **THE CLAIMS ARE NOVEL UNDER 35 U.S.C. § 102(b)**

Claims 55-71, 80-84 and 86-95 are rejected under 35 USC 102(e) as allegedly anticipated by Drstrup (US20030138403). The Examiner asserts that Drstrup teaches a formulation that is the same as the invention of claim 55. In particular, the Examiner takes the position that Drstrup teaches PEG conjugated IFN- $\beta$  and variants thereof, in a buffered formulation with pH 5.5 (citing to Example 5), and that IFN- $\beta$  encompasses IFN- $\beta$ -1b (citing to Drstrup ¶0022).

Applicants respectfully disagree. In order to maintain a novelty rejection, the Patent Office must consider the claims as a whole. Claim 55 requires an interferon-beta 1b conjugated to a polyalkylene oxide polymer, in an excipient and in a buffer solution, with a pH ranging from about 3 to about 5. While Drstrup does mention variants of IFN- $\beta$ , Drstrup points only to IFN- $\beta$ -1a as preferred (¶0215) but is silent as to IFN- $\beta$ -1b as part of the Drstrup formulation. Thus, "variants of IFN- $\beta$ " represents a generic disclosure that fails to anticipate the instantly claimed invention, with IFN- $\beta$ -1b, with the required specificity. *See* the discussion *In re Meyer* at MPEP 2131.02:

*In re Meyer*, 599 F.2d 1026, 202 USPQ 175 (CCPA 1979) (A reference disclosing "alkaline chlorine or bromine solution" embraces a large number of species and cannot be said to anticipate claims to "alkali metal hypochlorite."); *Akzo N.V. v. International Trade Comm'n*, 808 F.2d 1471, 1 USPQ2d 1241 (Fed. Cir. 1986) (Claims to a process for making aramid fibers using a 98% solution of sulfuric acid were not anticipated by a reference which disclosed using sulfuric acid solution but which did not disclose using a 98% concentrated sulfuric acid solution.).

Here, as in *Meyer* or *Akzo N.V.* the description of IFN- $\beta$  variants embraces a myriad of possible proteins. There is nothing that would enable the artisan to select IFN- $\beta$ -1b, in particular, for the claimed composition. The reason for this is that IFN- $\beta$ -1a is the more potent of the IFN- $\beta$  species, relative to IFN- $\beta$ -1b, and as discussed in greater detail in the response under 35 USC 103, the ordinary artisan, including Drstrup, would not have thought to try IFN- $\beta$ -1b. Thus, Drstrup would have failed to enable the claimed invention, and it is therefore

respectfully submitted that Drustrup fails to anticipate any of the pending claims.

For all of these reasons, reconsideration and withdrawal of this ground of rejection is respectfully requested.

**THE CLAIMS ARE NONOBVIOUS UNDER 35 U.S.C. § 103(a)**

The Examiner has set forth three different rejections under 35 USC 103(a).

1. Claim 85 was rejected under 35 U.S.C. 103(a) as allegedly unpatentable over Drustrup (US 20030138403).

2. Claims 74, 76-79, and 96-98 were rejected under 35 U.S.C. 103(a) as being unpatentable over Drustrup (US 20030138403) in view of McManus *et al* ("McManus" - US 20070166277).

3. Claim 75 was rejected under 35 U.S.C. 103(a) as being unpatentable over Drustrup (US 20030138403) in view of Saifer *et al* ("Saifer" - US 20040126361 - cited in the IDS received on 12/22/2006).

Applicants respectfully disagree.

1. The Examiner argues that Drustrup discloses IFN- $\beta$ -1b formulations comprising IFN- $\beta$  conjugated to PEG at 12 kDa, mannitol, and acetate buffer (as recited by claim 85). The Examiner further argues that it would have been obvious to optimize the claimed concentrations and pH ranges to arrive at the invention of claim 85. However, it is respectfully submitted, for all of the reasons given above, in the response to the novelty rejection, that Drustrup does not, in fact, disclose or suggest IFN- $\beta$ -1b. Instead, IFN- $\beta$ -1b is hidden among many potential variants of IFN- $\beta$ .

Further, the claimed invention is clearly nonobvious based on the teachings of the art. The Examiner's attention is respectfully directed to an article by Pepinsky et al., 2001, The Journal of Pharm. and Exper. Ther. 297(3): 1059-1066 (IDS dated 8/23/2006 Ref. No. A33). Pepinsky tested the potency of PEGylated IFN beta 1a. In summary, Pepinsky teaches that IFN-beta 1a is considered to be the more potent interferon, relative to IFN-beta 1b, but Pepinsky also teaches that PEGylated IFN beta 1a performed poorly. As described in the Pepinsky text bridging pages 1063-1064,

In selecting the 20-kDa PEG aldehyde adduct, we first screened a variety of sized PEGs for their effects on pharmacokinetics and activity in the antiviral assay. Lower molecular weight PEG aldehyde IFN- $\beta$ -1a conjugates were fully active, but failed to produce the desired enhancement in pharmacokinetic properties. Higher molecular weight forms, in contrast, which should further improve the pharmacokinetic properties of the molecule, compromised activity. (Underline added for emphasis).

Thus, it would not have been expected that the less potent IFN beta 1b would have provided good kinetics and retention of potency when PEGylated, relative to the PEGylated IFN beta 1a of Pepinsky. See, for example, page 6 of the instant patent application, last full paragraph and Example 5H, showing retained antiviral activity (compare to Pepinsky).

2. The Examiner argues that while Drustrup is silent as to the elected species of polyalkylene oxide polymer of claims 74, 76-79, and 96-98, this deficiency is remedied by McManus. As noted for the response to the first obviousness rejection, Drustrup does not, in fact, disclose or suggest IFN- $\beta$ -1b, and the teachings of Pepinsky would have taught away from employing IFN- $\beta$ -1b, in any combination of Drustrop and McMannus, in the instant invention.

3. The Examiner argues that while Drustrup is silent as to the SEQ ID NO: 1 of claim 75, this deficiency is remedied by Saifer. As noted for the response to the first obviousness rejection, Drustrup does not, in fact, disclose or suggest IFN- $\beta$ -1b, and the teachings of Pepinsky would have taught away from employing IFN- $\beta$ -1b, in any combination of Drustrop and Saifer, in the instant invention.

For all of these reasons, it is respectfully submitted that all of the foregoing rejections under 35 USC 103(a) be reconsidered and withdrawn.

### **FEES**

No fees are believed to be owed for entry of the instant amendment. However, in the event that it is determined that any fee is required, the Commissioner is authorized to treat this paper as the required authorization, and to charge or credit any required fee to Deposit Account No. 02-2275.

This Amendment is believed to be timely submitted. However, in the event that it is determined that any additional extension of time is required, the Commissioner is authorized to treat this paper as the required petition for extension of time, and to charge any required fee to Deposit Account No. 02-2275.

Pursuant to 37 C.F.R. 1.136(a)(3), please treat this and any concurrent or future reply in this application that requires a petition for an extension of time for its timely submission as incorporating a petition for extension of time for the appropriate length of time. The fee associated therewith is to be charged to Deposit Account No. 02-2275.

**CONCLUSION**

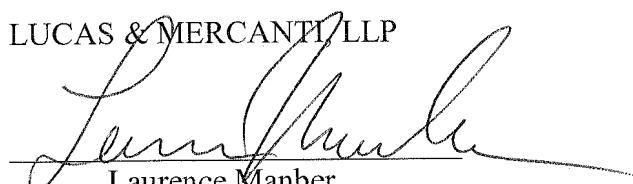
In view of the actions taken and arguments presented, it is respectfully submitted that each and every one of the matters raised by the Examiner have been addressed by the present amendment and that the present application is now in condition for allowance.

An early and favorable action on the merits is earnestly solicited. Applicants also respectfully request the Examiner to contact the undersigned to resolve any questions or issues that might remain.

Respectfully submitted,

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